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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/584,378	09/04/2007	Neil Berinstein	API-03-17-PCT-US	9064

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EXAMINER	
SINGH, ANOOP KUMAR	
ART UNIT	PAPER NUMBER
1632	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/584,378	BERINSTEIN ET AL.	
	Examiner	Art Unit	
	ANOOP SINGH	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 November 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *40-49,51 and 60* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *40-49, 51, 60* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's response to restriction requirement filed on November 5, 2009 has been received and entered. Applicants have amended claims 40 and 46, while claims 1-39, 50, 52-59 have been canceled. Claim 60 has been newly added that is generally directed to the elected invention. Applicants preliminary amendments to the specification filed September 4, 2007 have been entered.

Currently, claims 40-49, 51, 60 are pending.

Election/Restrictions

Applicant's election of claims 40-49, 51-57 and 60 in the reply filed on November 5, 2009 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)). Applicant's election with traverse of species avipox, SEQ ID NO: 4 as modified CEA and B7.1 as co-stimulatory molecule are acknowledged. Upon further consideration restriction requirement between different species is hereby withdrawn and all the species of virus and co-stimulatory molecule is hereby rejoined with the elected species.

Claims 40-49, 51 and 60 are under consideration.

Information Disclosure Statement

The listing of references in the specification is not a proper information disclosure statement. 37 CFR 1.98(b) requires a list of all patents, publications, or other information submitted for consideration by the Office, and MPEP § 609.04(a) states, "the list may not be incorporated into the specification but must be submitted in a separate paper." Therefore, unless the references have been cited by the examiner on form PTO-892, they have not been considered. In the instant case, applicants have cited multiple references in the specification but they have not been considered by the Examiner as no copy of any of the publication is provided.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 40-42, 45, 47, 49, 51 and 60 rejected under 35 U.S.C. 103(a) as being unpatentable over Herlyn et al. (WO/1998/ 29556, 7/9/1998), Szala et al (Proc. Natl. Acad. Sci. U.S.A. 87, 3542-3546, 1990), Warnaar et al (WO 1997/15597, dated 05/1/1997) and Kelly et al (US Patent 6,872,704, dated 3/29/2005, filed on 10/9/2002).

Claims are directed to an expression vector comprising nucleic acid sequences encoding modified KSA (SEQ ID NO: 15), wherein the vector is a plasmid or a viral vector. Claim 42 limits the expression vector of claim 41 wherein the viral vector is selected from the group consisting of poxvirus, adenovirus, retrovirus, herpesvirus, and adeno-associated virus subsequently limiting to avipox,. Claim 44 limits the vector of claim 43, wherein the poxvirus is selected from the group consisting of NYVAC, ALVAC, and ALVAC (2). Claim 49 is directed to a composition comprising an expression vector of claim 40 in a pharmaceutically acceptable carrier. Claim 51 is directed to an isolated DNA molecule encoding SEQ ID NO: 15, while claim 60 is drawn to an isolated nucleic acid molecule comprising SEQ ID NO: 20.

With respect to claims 40-42, 45, 47, 51, 60 Herlyn et al. teach a recombinant adenovirus comprising a nucleic acid encoding GA733-2/KSA for the induction of immune response as well as cytolytic response (see example 1-3). It should be noted that the GA733-2/KSA protein sequence disclosed by Herlyn et al. has ~99.7% homology with the sequence ID NO: 15 as evidenced by the teaching of Szala et al (see figure 4 and sequence search results). With respect to claims 45, Herlyn et al. teach the composition comprising an adenovirus comprising a nucleic acid encoding GA733-2/KSA may further comprises a DNA fragment encoding more than one antigens associated with a colorectal tumor and such antigens are expressed when cells are infected by the recombinant adenovirus (see claim 5 of '556). It is further disclosed that the composition further comprises at least one additional tumor associated antigen CEA or nucleic

acid encoding co-stimulatory component (see claims 2, 5 and 16 in Herlyn et al) meeting the limitation of the claims 45 and 47 respectively. Regarding claim 49, Herlyn et al. teach a pharmaceutical composition comprising a recombinant adenovirus comprising a nucleic acid encoding GA733-2/KSA for the induction of immune response (see claim 6-10 of '556). Herlyn et al teach a composition comprising an expression vector comprising a nucleic acid encoding KSA useful for immunizing a host, but differ from claimed invention by not disclosing Ile184V mutant in order to increase the capacity of the antigen to generate immune response by increasing the ability of KSA to bind MHC molecule.

Warnaar et al disclose KSA-derived peptides binding to HLA molecule comprise Ile184 (see SEQ ID NO: 3 and claims 4, 7 of '597). It is also disclosed that the one or more of the residue from amino acid ILYENNVIT (amino acid residue 184-192 of SEQ ID NO; 15) are replaced by an alternative residue. Warnaar differ form claimed invention by not disclosing substitution of amino acid Ile 184 with Val. However, conservative substitution of amino acid Isoleucine with Valine was routinely used and known in prior art as evidenced by Kelly et al (see col. 40, table A and B).

Therefore, it would have been *prima facie* obvious for a person of ordinary skill in the art to combine the teachings of Herlyn et al., Warnaar et al. to modify the KSA sequence at any one of the amino acid 184-192 using conservative substitution, as a matter of design choice, in a composition comprising nucleic acid encoding KSA, as instantly claimed, with a reasonable expectation of success, at the time of the instant invention. Said design choice amounting to combining prior art elements according to known methods to yield predictable results. One of ordinary skill in the art would be motivated to modify the sequence of KSA in order to increase the capacity of the antigen to generate immune response by increasing the ability of KSA to bind MHC molecule. One of skill in the art would have been expected to have a reasonable expectation of success in modifying amino acid sequence of KSA by conservative substitution at position Ile184 with Val, because the art teaches successful conservative substitution of amino acid Ile with Val. Thus, it would have only required routine experimentation for one of ordinary skill in the art to modify the amino acid sequence disclosed by Herlyn et al to further increase the capacity of the antigen to generate immune response by increasing the ability of KSA to bind MHC molecule. It should be noted that the *KSR* case forecloses the argument that a **specific**

teaching, suggestion, or motivation is required to support a finding of obviousness See the recent Board decision *Ex parte Smith*, --USPQ2d--, slip op. at 20, (Bd. Pat. App. & Interf. June 25, 2007) (citing *KSR*, 82 USPQ2d at 1396) (available at http: www. uspto.gov/web/offices/dcom/bpai/prec/fd071925.pdf).

Claims 40-49, 51 and 60 are rejected under 35 U.S.C. 103(a) as being unpatentable over Herlyn et al. (WO/1998/ 29556, 7/9/1998), Szala et al (Proc. Natl. Acad. Sci. U.S.A. 87, 3542-3546, 1990), Warnaar et al (WO 1997/15597, dated 05/1/1997), Kelly et al (US Patent 6872,704, dated 3/29/2005, filed on 10/9/2002) as applied above, and further in view of Schlom et al (WO/2000/34494, dated 06/15/2000) and Berinstein et al (WO/2001/30382, dated 5/3/2001).

Claim 40-42, 45, 49, 51 and 60 are included again in the rejection in order to address the specific limitation of other co-stimulatory molecule and virus being avipox.

The references of Herlyn, Szala, Warnaar et al and Kelly have been discussed above and relied in same manner here. The combination of reference teaches an expression vector comprising nucleic acid sequence encoding modified KSA set forth as SEQ ID NO: 15. The combination of references teach a adenovirus vector comprising a nucleic acid encoding KSA, wherein KSA is modified at position 184 by conservative amino acid substitution to increase the ability of KSA to bind MHC molecule. It is noted that the combination of references teach the composition further comprises at least one additional tumor associated antigen CEA or nucleic acid encoding co-stimulatory component (see claims 2, 5 and 16 in Herlyn et al). However, combination of references differs from claimed invention by not disclosing using avipox as viral vector or B7.1 as co-stimulatory molecule.

However, use of avipox as viral vector and B7.1 as co-stimulatory molecule in immunization was routine and known in prior art. For instance, Schlom et al cure the deficiency by teaching a recombinant vector encoding and expressing at least one co –stimulatory molecule and further comprising a gene encoding one or more target antigens (See abstract and claim 1, 12, 14, 15 and 17 of '494), wherein the recombinant vector is poxvirus that is avipox or NYVAC (see claim 12-15 of '494). It is also disclosed that the tumor specific target antigen may be CEA,

MUC-1, normal or point mutated p53 or KSA (see claim 26 of '494), while co-stimulatory molecule may be selected from a group consisting of B7.1, LFA-3 and ICAM-1 (see claim 4 of'494) meeting the limitation of claims 42-48. It is noted that modified CEA nucleic acid and protein sequence (SEQ ID NO: 111, 112) disclosed by Berinstein et al has 100% sequence homology with SEQ ID No: 5.

Therefore, it would have been *prima facie* obvious for a person of ordinary skill in the art to combine the teachings of Herlyn et al., Szala, Warnaar et al. to modify the expression vector comprising a nucleic acid sequence encoding modified KSA by substituting adenoviral vector and co-stimulatory molecule with functionally equivalent avipox virus and other co-stimulatory molecule as disclosed by Schlom, as a matter of design choice, in the composition comprising nucleic acid encoding SEQ ID NO: 15 and further comprising at least one nucleic acid encoding co-stimulatory molecule, as instantly claimed, with a reasonable expectation of success, at the time of the instant invention. Said design choice amounting to combining prior art elements according to known methods to yield predictable results. One of skill in the art would have been expected to have a reasonable expectation of success in using avipox virus and other co-stimulatory molecule such as B7.1, LFA-3 and ICAM-1 because the art teaches routine and successful use of avipox virus and other co-stimulatory molecule to enhance immune response specifically to a target antigen as disclosed by Schlom. It should be noted that the *KSR* case forecloses the argument that a **specific** teaching, suggestion, or motivation is required to support a finding of obviousness See the recent Board decision *Ex parte Smith*, --USPQ2d--, slip op. at 20, (Bd. Pat. App. & Interf. June 25, 2007) (citing *KSR*, 82 USPQ2d at 1396) (available at http: www. uspto.gov/web/offices/dcom/bpai/prec/fd071925.pdf).

Conclusion

No claims allowed.

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. Trojan et al (Cancer Research, 2001, 61, 12, 4761-4765) teaches KSA derived MHC-1 binding peptides comprising conservative single amino acid mutation that increases binding

affinity to HLA-A2, thereby allowing generation of cytotoxic T cell leading to increased target cells killing.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to ANOOP SINGH whose telephone number is (571)272-3306. The examiner can normally be reached on 9:00AM-5:30PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Peter Paras can be reached on (571) 272- 4517. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Anoop Singh/
Examiner, Art Unit 1632